The Japp-Klingemann Reaction of Diethyl Benzoylsuccinate

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An extensive review of the Japp-Klingemann reaction has been made by Phillips.[1] It is well known that the coupling reaction of a diazotized aniline with a methinyl carbon gives an unstable azo compound, which then decomposes to give a hydrazone, whereas the coupling product between the same diazotized aniline and a methylene carbon is not an azo compound, but a hydrazone.

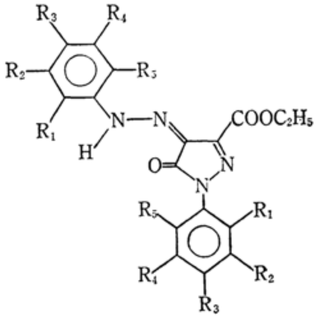
A previous paper[2] has presented a formation of 2-pyrazoline-5-one dye in an attempt to prepare the diethyl α-ketosuccinate phenylhydrazone by coupling diazotized aniline to diethyl acetylsuccinate in an alkaline medium.

This paper will describe the results obtained from the coupling reaction of diazotized anilines with diethyl benzoylsuccinate (I). The succinate I was prepared from ethyl sodiobenzoylacetate and ethyl monochloroacetate in boiling ethanol.

When benzenediazonium chloride reacted with I in ethanol containing sodium hydroxide, a product melting at 151—152°C was obtained; this product showed different behavior from expected diethyl α-ketosuccinate phenylhydrazone in melting point (76—78°C) or in debenzoylation. The analysis has suggested that this coupling product is 1-phenyl-3-ethoxycarbonyl-4-phenylhydrzaono-2-pyrazolin-5-one (IIa). The structure of the coupling product was further established by independent synthesis from the coupling reaction of benzenediazonium chloride with 1-phenyl-3-ethoxycarbonyl-2-pyrazolin-5-one.

Similarly, the reaction of I with two equivalents

TABLE I. 1-ARYL-3-ETHOXYCARBONYL-4-ARYLHYDRAZONO-2-PYRAZOLIN-5-ONES OBTAINED



Compound	R_1	R_2	R_3	R_4	R_5	Yield %	M.p. °C[c]	Lit. m.p. °C	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
										Calcd.	Found	Calcd.	Found	Calcd.	Found
IIa	H	H	H	H	H	42	151—2	152[a]	$C_{18}H_{16}O_3N_4$	64.27	64.84	4.80	4.55	16.67	16.85
IIb	Me	H	H	H	H	45	112—3	145[b]	$C_{20}H_{20}O_3N_4$	65.92	65.98	5.53	5.36	15.38	15.41
IIc	H	Me	H	H	H	38	141—2	146—7[b]	$C_{20}H_{20}O_3N_4$	65.92	66.17	5.53	5.37	15.38	15.28
IId	H	H	Me	H	H	38	142—3	143[b]	$C_{20}H_{20}O_3N_4$	65.92	65.91	5.53	5.24	15.38	15.59
IIe	H	OMe	H	H	H	39	124—5		$C_{20}H_{20}O_5N_4$	60.60	60.64	5.09	5.01	14.14	14.39
IIf	H	H	OMe	H	H	39	163—4		$C_{20}H_{20}O_5N_4$	60.60	60.80	5.09	5.06	14.14	14.21
IIg	H	Br	H	H	H	42	166—7		$C_{18}H_{14}O_3N_4Br_2$	43.73	43.58	2.83	2.67	11.34	11.29
IIh	Me	Me	H	H	H	36	163—4		$C_{22}H_{24}O_3N_4$	67.33	67.51	6.16	6.05	14.28	14.43
IIi	Me	H	Me	H	H	25	158—9		$C_{22}H_{24}O_3N_4$	67.33	67.38	6.16	5.86	14.28	14.43
IIj	Me	H	H	Me	H	36	137—8		$C_{22}H_{24}O_3N_4$	67.33	67.37	6.16	5.91	14.28	14.42
IIk	Me	H	H	H	Me	36	130—1		$C_{22}H_{24}O_3N_4$	67.33	67.24	6.16	6.02	14.28	14.49

a) S. Astin and H. L. Riley, *J. Chem. Soc.*, **1934**, 844.
b) V. V. Feofilaktov and T. N. Ivanova, *J. Gen. Chem.* (*U. S. S. R.*), **25**, 111 (1955).
c) All melting points are uncorrected.

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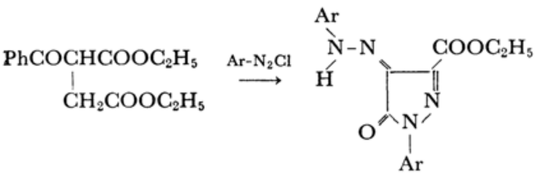
1) R. R. Phillips, "Organic Reaction," Vol. 10, John Wiley & Sons, New York, N. Y. (1959), Chapter 2.

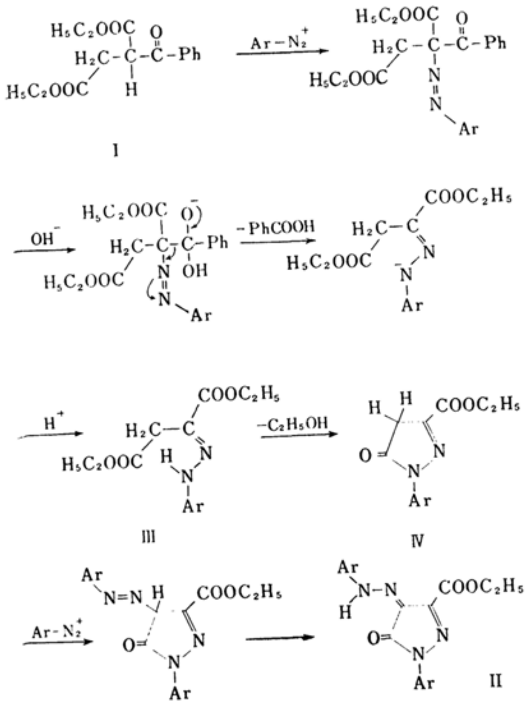
2) H. Yasuda, *J. Sci. Res. Inst. (Tokyo)*, **30**, 199 (1954).

of the respective diazotized anilines gave the corresponding dyes (II) in varying yields, ranging from 25 and 46% respectively. In each case, the remainder of the reaction mixture was a non-distillable, resinous material which could not be identified further. The relatively low yields may be due to the formation of appreciable amounts of the resinous material during the coupling reaction. This reaction is illustrated in the following equations.



I II

Very recently,[3] the actual structures of 2-pyrazolin-5-one dyes, in which 4-positions are coupled with various diazotized anilines, have been shown to be the hydrazone-keto form and not an azo-keto or an azo-enol form. Table I summarizes the yield and other data obtained in the Japp-Klingemann reaction of I with eleven diazotized anilines.



The mechanism of the formation of the pyrazolinone dyes (II) from I and diazotized anilines apparently involves azo coupling on the α-methinyl carbon, thus forming an intermediate diethyl α-ketosuccinate arylhydrazones (III) via debenzoylation. This intermediate is expected to undergo an intramolecular cyclization by the elimination of one molecule of ethanol, thus giving 1-aryl-3-ethoxycarbonyl-2-pyrazoline-5-ones (IV). Compound IV, once formed, reacts with another molecule of diazotized aniline to give the pyrazolinone dyes (II). The probable scheme is illustrated as follows.

Experimental

General Procedure for the Japp-Klingemann Reaction.—To a mechanically-stirred solution of 1 g. of sodium hydroxide in 50 ml. of 90% ethanol, 2 g. (0.00719 mol.) of diethyl benzoylsuccinate was added; the mixture was then cooled to 0°C. A diazonium solution (prepared by dissolving 0.0719 mol. of the appropriate aniline in 15 ml. of 2 N hydrochloric acid, cooling it to 0°C, and adding a saturated aqueous solution of 1.1 g. of sodium nitrite) was slowly stirred in mechanically. During the addition, a colored, oily, resinous matter separated. This matter was collected in a suitable manner and poured into a stirred mixture of 30 ml. of acetone and 30 ml. of ethanol. After the stirring had continued for 30 min., the mixture was diluted with water until clouding persisted. The colored solid which separated was collected, washed with methanol-water, and recrystallized from dioxane-water. The results are listed in Table I.

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3) H. Yasuda and H. Midorikawa, *J. Org. Chem.*, in printing.